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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,358	10/02/2003	Karine Vidal	88265-6852	8288

29157 7590 10/13/2006

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,358	VIDAL ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-19* is/are pending in the application.

4a) Of the above claim(s) *12-16* is/are withdrawn from consideration.

5)☒ Claim(s) *17* is/are allowed.

6)☒ Claim(s) *1,3-11,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1 and 3-19 are pending.

Applicants' amendment filed July 31, 2006 is acknowledged. Applicant's response has been fully considered. Claims 17 and 18 have been amended. Claims 12-16 are non-elected inventions and withdrawn from consideration. Therefore, claims 1, 3-11, and 17-19 are examined.

Withdrawn Claim Rejections - 35 USC § 102

2. The previous rejection of claim 17 under 35 U.S.C. 102(b) as being anticipated by D'Ostilio *et al.* (Clinical and Experimental Immunology 104, 543-546 (June 1996)), is withdrawn in view of applicants' amendment to the claim, and applicant's response at page 7 in the amendment filed July 31, 2006.

3. The previous rejection of claim 18 under 35 U.S.C. 102(b) as being anticipated by Boyle *et al.* (U.S. Patent 6,015,938, January 18, 2000), is withdrawn in view of applicants' amendment to the claim, and applicant's response at pages 7-8 in the amendment filed July 31, 2006.

Maintained Objection to the Specification

4. The specification cites "The OPG of the present invention, i.e. in a form obtainable from milk source, has a polypeptide sequence as identified by SEQ ID. No. 1 and exhibits sizes of about 80, 130 and 200 kDa, respectively, which differs from that obtained by recombinant means (i.e., 55 kDa)." at page 5, lines 8-10 (see also page 12, lines 11-13). However, Fig. 2, the Western blot analysis of human milk fractions under reduced conditions using 10% SDS-gel (page 9, lines 19-25), only shows the band of 130 kDa for various milk fractions containing

OPG, it does not show the bands of 80 and 200 kDa for these milk fractions, nor indicates the band of 55 kDa for recombinant OPG. Applicant has responded the objection along with the rejection under 35 U.S.C. 112, first paragraph as shown below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Previous rejection of claims 1, 3-11 and 19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained, and claim 18 is added to the rejection. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-11, 18 and 19 are directed to osteoprotegerin isolated from human or bovine milk or colostrums, or obtained from recombination methods in cells, wherein the osteoprotegerin includes a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa (claims 1, 3 and 19); a food material, an enteral composition or a pharmaceutical composition comprising the osteoprotegerin (claims 4-7 and 11); or a method of making a food material, an enteral composition or a pharmaceutical composition by adding the osteoprotegerin (claims 8-10 and 18). While the specification cites the OPG of the present invention, i.e. in a form obtainable from milk source, has a polypeptide sequence as identified by SEQ ID NO: 1 and exhibits sizes of about 80, 130 and 200 kDa, respectively, which differs from that (i.e., 55 kDa) obtained by recombinant means (see page 5,

lines 8-10; page 12, lines 11-13); and the OPG of the present invention may be isolated from milk sources or prepared by recombinant means (page 8, lines 3-8), the specification does not show the OPG obtained from various milk fractions or by recombinant means has a molecular weight of about 80, 130 and 200 kDa (see the bands in Fig. 2). The specification only shows a band of molecular weight of about 130 kDa for various milk fractions and recombinant OPG, and there is no 55 kDa band for recombinant OPG in the western blot (Fig. 2). The lack of description for the osteoprotegerin isolated from human or bovine milk or colostrums, or obtained by recombinant means and having a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Response to Arguments

Applicants indicate Fig. 2 shows the results of an example of a Western Blot analysis performed by Applicants under the conditions as indicated. As a result, it is commonly observed throughout the experimental work that a specific analytical experiment can reveal the presence of one compound clearly, while less clearly revealing the presence of another compound. Regarding bands allegedly lacking for a protein having 200 kDa, Applicants submit that a band, which is weaker in appearance but nevertheless clearly visible, is present in the region of about 200 kDa in Fig. 2. Thus, the present inventors were at least in the possession of a protein characterized by the sequence having a respective molecular weight of 130 and 200 kDa.

Moreover, during a Western Blot analysis chemical reactions such as; for example, dimerisations and trimerisations may occur, such chemical reactions could reasonably explain the absence of a band for recombinant OPG at 55 kDa and the presence of bands having a higher molecular weight, e.g., OPG is well known to dimerize to a dimer of 110 kDa (See page 12, lines 11-13 of the specification). Because Fig. 2 illustrates that, under the experimental conditions chosen for this Western blot analysis (e.g. different from the conditions prevailing in milk) chemical reactions can occur giving rise to compounds of higher molecular weight, it can be reasonably concluded that the OPG of 80 kDa (i.e. the least glycosylated OPG) may have been subjected to the same chemical reactions that potentially occurred in the case of the recombinant OPG of 55 kDa. The absence of such a clearly visible band for OPG at 80 kDa in the particular experiment does not mean it does not exist but reflects the routine variation using different experimental conditions encountered by Applicants when conceiving and reducing to practice the present invention. Furthermore, the specification states that the OPG of the present invention may be obtained from a milk source, derived from a mammal, in particular from human or bovine milk or colostrum. Human milk OPG has an amino acid sequence of 380 aa and exhibits a molecular weight of approximately 80, 130 and 200 kda when compared to protein markers which were used as molecular weight standards (e.g. BioRad). Applicants provide further details regarding the detected bands in the Western Blot Analysis (see page 12, lines 10-13). Because these claimed elements are sufficiently described in the specification, one having ordinary skill in the art would understand that Applicants had possession of the claimed subject matter even without additional figures (pages 5-7 of the response).

Applicants' response has been fully considered, however, the arguments are not found persuasive because of the following reasons. While the specification indicates the milk bands in the Western Blot Analysis were detected at approximately 80, 130 and 200 kDa (see page 5, lines 8-10; page 12, lines 10-13), Fig. 2 only shows a clear 130 kDa band for various milk fractions and recombinant OPG in the Western blot analysis. It appears there is a band of 110 kDa for the recombinant OPG, which may be due to dimerization of 55 kDa as indicated in applicants' response (see above), however, there are no higher molecular weight bands (e.g., 160 or 240 kda) indicating the dimerization and trimerization of 80 kDa. Although applicant has argued there is a weak band of 200 kDa in Fig. 2, it is not clearly visible from the appearance of the bands. While the specification indicates the OPG from milk source were detected at approximately 80, 130 and 200 kDa (page 12. lines 10-12), and OPG prepared by recombinant means may yield a glycoslation pattern as found in the milk OPG (page 8, lines 3-7), the absence of such a band at 80 kDa for recombinant OPG or various milk fractions in Fig. 2 does not fully support the glycosylation pattern of OPG. Therefore, applicants have failed to sufficiently describe the claimed invention, that is the osteoprotegerin includes a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa.

Conclusion

6. Claims 1, 3-11, and 18-19 are rejected; and it appears that claim 17 is free of art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
October 4, 2006